Modern Concepts of Cardiovascular Disease

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HAZARDS IN THE TREATMENT OF CARDIAC DECOMPENSATION*

One aspect of the treatment of congestive heart failure that deserves repeated emphasis is the harm that may be caused by therapy injudiciously or erroneously applied.

Digitalis

The common manifestations of digitalis intoxication — that is, nausea and vomiting, bigeminy and heart block — are well known. The possible occurrence of less common symptoms, such as diarrhea and visual disturbances, should be remembered. Some rare cardiac disorders caused by administration of excessive amounts of digitalis must also be borne in mind. Digitalis has strong vagal effects, one of which may be the production of auricular fibrillation. In other cases the vagal action may cause slowing of the heart rate to below 50 per minute, with the resultant precipitation of Stokes-Adams attacks. This phenomenon is rare but is most likely to occur in patients who are unable to increase the cardiac stroke output markedly, owing to severe myocardial disease or valvular stenosis. Another aspect of digitalis therapy that might be mentioned in passing is an error of omission rather than of commission: many physicians forget that some patients become de-digitalized gradually, unless redigitalized (cautiously) three or four times a year.

Bed Rest

There is conflict among authorities concerning the value and harm of bed rest for patients with congestive heart failure. The purpose of rest should be understood as avoidance of exertion, and not the maintenance of complete immobility or of any specific position. Few if any cardiologic authorities ever recommend rigid restriction of patient to bed; a comfortable reclining chair serves as well. However, clinical experience shows that unduly prolonged rest causes muscular flabbiness and often psychologic changes that may be disabling.

If these limitations are accepted, there is no reason to derogate traditional ideas about rest in the treatment of cardiac decompensation. The belief that bed rest of itself causes deep femoral phlebitis and subsequent pulmonary infarction is not securely founded in controlled observation; other known factors that should be considered as favoring the development of this condition are extreme degrees of stasis associated with excessive use of barbiturate drugs, hemoconcentration during overenthusiastic diuretic therapy and changes in blood clotting caused by barbiturate drugs or by severe physical or emotional shock or discomfort. The problem of femoral phlebitis in the bedridden requires much study, and statements that the bed alone is to blame are as yet unproved. In this connection it is important to bear in mind that bed rest in the waking state may have markedly different effects from best rest during sleep or stupor.

Morphine

The immediate and strikingly beneficial effect of morphine on cardiac dyspnea is well known. This action is presumably due to amelioration of discomfort in general and also to diminution in respiratory activity in some cases. Untoward effects are also well known; these include excessive — in some cases, fatal — depression of respiration in chronic cor pulmonale, vomiting or cutaneous itching in sensitive persons and impairment of bladder function in patients with enlarged prostate glands.

Other undesirable consequences of the action of morphine include inhibiting mercurial diuresis, and a hypotensive effect. Morphine in

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doses of about 15 mg. has no effect on the circulation in recumbent patients; however, when subjects given morphine are tilted up with feet dependent, a hypotensive syncopal attack may occur. This same effect may cause collapse in patients with myocardial infarction or pulmonary edema who are placed with the head up and feet hanging.

Oxygen

The use of oxygen in the treatment of cardiovascular disease is usually beneficial but occasionally may have harmful effects. Mixtures containing 90 to 100 per cent of oxygen may cause a decrease in vital capacity when administered continuously for twenty-four to thirty-six hours. The gas in high concentration is also irritating to the respiratory mucosa. In occasional cases it may favor the development of atelectasis. This phenomenon is apparently owing to the washing out of the nitrogen in the pulmonary alveoli — a process that requires less than seven minutes in the normal lung and less than fifteen, as a rule, in the abnormal lung. Alveoli containing no nitrogen will, if temporarily blocked by secretion, collapse markedly when the oxygen in them is rapidly absorbed; the presence of less readily absorbable nitrogen in alveoli normally permits only a slight amount of immediate alveolar collapse when the small bronchi are temporarily plugged. A rare complication of the prolonged use of high concentrations of oxygen is the vasomotor collapse that may occur when the patient suddenly resumes breathing room air; oxygen in high concentration has a systemic vasoconstrictor effect (of unknown mechanism), and during its action normal vasomotor mechanisms may be depressed, leaving the patient without protection against hypotension when the oxygen is removed.

The harmful effects of oxygen therapy in cor pulmonale are also worthy of comment; they may be precipitated in this condition by concentrations as low as 40 per cent. Chronic anoxia and carbon dioxide retention of severe degree are present in cor pulmonale. The respiratory center becomes accustomed to this degree of hypercarbia in only a few days, and the excess carbon dioxide in the blood ceases to act as an effective respiratory stimulant; respiration is maintained largely by the stimulus of anoxia. Relieving the anoxia by means of oxygen therapy depresses respiration to such a degree that carbon dioxide retention increases markedly. The resulting acidosis (or possibly the carbon dioxide itself, which in high concentration is a narcotic) causes coma, or in some cases confusional psychoses. Another acidotic mechanism — one causing tissue acidosis — acts in patients given excessive amounts of oxygen. The transport of carbon dioxide away from the tissues depends in large measure on the development of basic properties in hemoglobin when it is changed from acid oxyhemoglobin to reduced hemoglobin. The therapeutic use of oxygen in high concentrations may cause so much of the gas to dissolve in the plasma that venous blood contains a decreased amount of the basic reduced hemoglobin; tissue carbon dioxide retention results. All the acidosis-producing effects of oxygen administration are rapidly reversed when room air is breathed.

Aminophylline

The action of aminophylline in causing gastric irritation needs no comment here. In addition, it is a potent relaxer of smooth muscle. It greatly relaxes constricted bronchi and has a less striking effect on the smooth muscle of blood vessels; its effects on other smooth muscle are negligible in doses used clinically. The drug must be given intravenously if a rapid dilatation of constricted bronchi is desired, as in cardiac asthma. The aim is to obtain a circulating concentration of the drug large enough to relax bronchial muscle but not enough to dilate vascular muscle. Rapid injection of aminophylline may cause so much vasodilatation as to precipitate collapse or even death. Slower but still excessively rapid injection may cause lesser degrees of peripheral arteriolar dilatation, resulting in an increase in cardiac output (and work) and the development of cardiac pain in patients with rigid coronary arteries. This reaction may at first seem paradoxical, since aminophylline is used for the treatment of anginal pain, being given by mouth, however, in doses far too small to cause generalized vasodilatation.

Ammonium Chloride

Ammonium chloride may cause gastric irritation, the manifestations of which may confuse the picture in a patient in the process of digitalization. This effect may be obviated by the use of enteric-coated tablets of the drug, but it must be remembered that in occasional cases this coating may not dissolve in the intestinal tract; a simple way to test this is to measure the urinary chloride output after the drug has been given.

The action of ammonium chloride as a diuretic given alone is largely based on the transformation of ammonium ion to urea, with the resulting liberation of chloride ion that carries sodium

with it as it is excreted. This mechanism ceases to act after a few days and the drug is excreted unchanged; the diuretic effect of ammonium chloride, never great, is only of short duration. However, the use of the drug is important in patients given mercurial injections, in that it prevents the development of excessively low blood chloride levels, thereby augmenting diuresis and reducing the tendency to refractoriness. When ammonium chloride is given to patients with impaired renal function, a significant rise in blood urea level occurs. It is not established that this is harmful. However, the giving of very large doses of the drug, such as 15 gm. a day to normal subjects or small amounts for long periods to patients with renal insufficiency, leads to the accumulation in the blood of ammonium ion in concentrations toxic to brain tissue; psychosis or coma may result.

The prolonged use of ammonium chloride in patients with renal insufficiency may also cause sufficiently severe acidosis to produce coma. Even the mild acidosis that regularly develops in patients given 8 to 10 gm. of ammonium chloride a day may have undesirable effects; cardiac output is increased, and a strain thereby imposed on the heart. The acidosis may aggravate dyspnea. In addition, acidosis has a metabolic effect, not well understood at present, consisting in a depression of carbohydrate utilization. This phenomenon may complicate the regulation of some diabetic patients and in all patients increases protein wastage. The occurence of protein deficiency in many patients with congestive heart failure is well known; it might be aggravated by the long-continued use of moderately large doses of ammonium chloride.

Mercurial Diuretics

The action of mercurial diuretics depends on their effect in inhibiting the reabsorption of chloride in the renal tubules; the increased output of chloride carries off base — chiefly sodium — and water. Frequent mercurial diureses may so markedly deplete the body of chloride as to prevent subsequent mercurial diuresis even though the patient is still edematous. The situation is easily remedied by the administration of ammonium chloride, 7 or 8 gm. of that substance being required to prevent a fall of blood chloride level during mercurial diuresis.

More serious is the development of the low-sodium syndrome, which is the result of frequent mercurial injections in a patient whose sodium intake is markedly restricted. Some patients with a lowered blood sodium concentration may become unresponsive to mercurial injections whereas others may continue to have fairly large diureses. In the latter a variety of syndromes develop — muscle cramps, confusion, stupor or a shock-like state usually unaccompanied by tachycardia. The treatment is to give a 5 per cent solution of sodium chloride intravenously, despite which an occasional patient may go on to die. Prevention of the syndrome merely involves limitation of excessively rigid salt restriction to cardiac patients who can be kept free of edema by this degree of restriction alone, without mercurial diureses.

The loss of chloride that occurs during mercurial diuresis carries off basic ions other than sodium. The loss of potassium and calcium is increased in patients depleted of sodium. The loss of calcium rarely reaches degrees sufficient to cause hypocalcemic tetany, but the depletion of body stores of potassium may be marked. Some patients actually excrete more potassium than sodium during diuresis induced while they are in a state of sodium depletion. It has been known for decades that skeletal muscle of patients with congestive heart failure contains abnormally low concentrations of potassium; whether the profound skeletal-muscle weakness of cardiac decompensation is related to this chemical change is at present a matter for conjecture. There is some evidence that potassium loss accentuates digitalis intoxication. The loss of potassium during mercurial diureses can be minimized by administration of generous amounts of fruit juices, which contain a good deal of potassium and little sodium.

The possibility of mercury poisoning need be mentioned only briefly. It occurs only — and usually in a mild form — in patients given mercurial diuretics by mouth.

Low-Salt Diets

Some patients in whom edema develops during congestive heart failure may be kept free of edema by means of rigid restriction of sodium intake without the use of mercurial diuretics. Skill is needed in the planning of these diets, to make them attractive and to ensure that the patients receive required amounts of animal protein and components of the vitamin B complex. Use of the Karell diet imposes additional deficiencies of calories, thiamine, vitamins A and C and iron.

Severe restriction of sodium intake combined with repeated injections of mercurial diuretics can be expected to lead to the low-sodium syndrome. Patients who require frequent mercurial diuresis should be advised not to restrict their salt intake excessively; extreme restriction is best

reserved for patients who can be kept free of edema without mercurial diureses.

Ion-Exchange Resins

The use of ion-exchange resins is not widespread at present but may become so. In addition to gastrointestinal upset and the acidosis caused by the ammonium chloride contained in some resins, the chief hazard is sodium depletion.

Abnormal Water Intake

Marked restriction of water intake was once practiced in the treatment of edema in cardiac disease. It is now known that this was of little help in preventing edema and might even favor its persistence owing to stimulation of the posterior lobe of the pituitary gland. In recent years forcing of fluids by mouth has been recommended by some, with the aim of obtaining the diuretic effect of water. However, it has long been known that water diuresis cannot be induced in edematous cardiac patients; excessive intake of water may produce vomiting and signs of water intoxication.

Anticoagulants

The use of anticoagulant drugs to counteract the tendency to the development of femoral phlebitis in congestive heart failure is not without hazard. The dangers of anticoagulant therapy are increased in the presence of hepatic disease; dosages should accordingly be smaller than usual in patients with engorged livers.

Tourniquets, Venesection and Positive-Pressure Respiration

Decreasing the venous return from the limbs by means of tourniquets helps to relieve pulmonary congestion and edema. However, the diminution in blood flow through the lungs is accompanied by a corresponding fall in the output of the left ventricle; in addition, the blood volume decreases as a result of increased filtration into the tissues of the extremities. Shock is sometimes precipitated by the use of tourniquets. Tourniquets also cause a marked reduction in cutaneous blood flow in the extremities and thereby impair heat dispersal; the use of tourniquets for several hours may induce a fever that may be misinterpreted. Another effect that may be misleading is a sudden increase in respiratory activity that occurs shortly after the tourniquets are released; this phenomenon is due to the entry into the circulation of blood containing large amounts of lactic acid and carbon dioxide accumulated during a period of stasis in the extremities. This brief period of hyperpnea should not be considered an indication for the reapplication of tourniquets.

Tourniquets commonly cause the development of edema in the extremities, owing to increased filtration from the obstructed vessels. In addition, some mechanism that causes over-all water retention apparently operates; this mechanism has not yet been defined. It is evident that prolonged use of tourniquets enhances peripheral edema and might theoretically favor the accumulation of pulmonary edema in one way while diminishing it in others.

Venesection and positive-pressure respiration decrease cardiac output and blood volume and thereby may precipitate or aggravate shock. The difficulty of performing venesection in patients in incipient or mild shock has saved many lives. Prolonged standing or sitting with legs dependent causes a decrease in blood volume (owing to increased filtration into the tissues of the legs) and in cardiac output and accordingly affords all the hazards as well as all the benefits of the application of tourniquets.

Discussion

In some localities cardiac patients are undertreated with digitalis and overtreated with the other measures used in congestive heart failure. It is evident that adequate treatment with digitalis minimizes the need for some of the procedures discussed here. It must be borne in mind that, except for digitalis, all therapy for cardiac decompensation is symptomatic and does not improve cardiac function (except indirectly by relief of anoxia in some cases); these treatments impose abnormalities that are different from but only partly opposite to those of the disease. It is not surprising, therefore, that use of the therapeutic agents discussed above may do harm at times. On the other hand, any harm done is usually the result of excessive or injudicious use of these agents; the well informed, alert physician can prevent these hazards or counteract them quickly when they occur.

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The opinions and conclusions expressed herein are those of the author and do not necessarily represent the official views of the Scientific Council of the American Heart Association.